REMARKS

Claims 2 – 4 and 15 and 16 are currently pending. Of these, Claims 15 and 16 are new. In the Office Action, Claims 2 – 4 were rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of Hoorn et al. (US 6,835,853) (hereinafter, "Hoorn").

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. Rejections of Claims 2 – 4.

The Examiner argues that Claims 2 – 4 would have been obvious over the Hoorn '853 patent. It is submitted that these rejections are not well taken. Claims 2 – 4 are directed to a purified reaction mixture formed from the alkylation of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide *with a molar excess* of 1-(2-bromoethoxy)- 2-ethoxybenzene. The purified reaction mixture as claimed is composed of at least 99.5% tamsulosin hydrochloride together with at least some measurable amount of undesired "overalkylated" side products or impurities.[1] These "overalkylated" impurities according to claims 15 and 16 include 5-(2-(bis-(2-(2-ethoxyphenoxy)ethyl)amino)propyl)-2- methoxybenzenesulphon-amide and N-(2-(2-ethoxyphenoxy)ethyl)-5-(2-(2-(2-ethoxyphenoxy)ethylamino)propyl)-2-methoxybenzenesulphonamide. According to Claims 2 – 4, the measurable amount of the overalkylated products in the mixture, after purification, is less than 0.1 %.

Once again, Applicants wish to stress that their claim requires a measurable amount of overalkylated compounds in the purified reaction mixture following reaction of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide with a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene; however, with a surprising result that the amount of overalkylated impurities in the crude reaction product (pre-purification) is significantly reduced when a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene is reacted with R-5-(2-aminopropyl)-2-

[1] These percentages are directed to the tamsulosin (together with reaction impurities or the like), non-solvent or non-diluent portion of the reaction mixture. That is, these percentages would be proportionally less for compositions that still contain one or more solvents or other diluents.

methoxybenzenesulphonamide. The fact that overalkylated impurities are much lower in the crude reaction product (and in the nature of their composition as well) according to the invention is surprising, unexpected, and counterintuitive since the presence of extra 1-(2-bromoethoxy)- 2-ethoxybenzene (as opposed to extra R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide, as taught by Hoorn) would seemingly provide more opportunities for the R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide to become overalkylated. Instead, Applicants have found the reverse to be true.

This cannot reasonably be said to be suggested by the information in Hoorn. While Hoorn mentions as one of several processes for the synthesis of tamsulosin the route of alkylation of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene (See column 14, lines 18 – 61), it is error to suppose that Hoorne discloses or suggests using a molar excess of the latter. If anything, Hoorn suggests the reverse.

In Example 2A, Hoorn uses an approximately 2 to 1 molar excess of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide over 1-(2-bromoethoxy)-2-ethoxybenzene. This is opposite to the direction taken by Applicants.

Thus, in effect, Hoorn would led a person of skill away from the subject matter of Claims 2 – 4. In this regard, the Appeal Board has recently determined that "[w]hen the prior art teaches away from a claimed solution, obviousness cannot be proven merely by showing that a known composition could have been modified by routine experimentation or solely on the expectation of success; it must be shown that those of ordinary skill in the art would have had some apparent reason to modify the known composition in a way that would result in the claimed composition." *See Ex parte Whalen*, 89 USPQ2d 1078 (BPAI 2008)

From this, coupled with what is apparent in terms of the chemistry involved, it is also plainly wrong to postulate that reversing the molar ratios of Hoorn to an opposite of what is "actually" used by Hoorn in Example 2A would be expected to yield the same amount and composition of impurities. It is especially erroneous to assume that a purified reaction mixture resulting from Hoorn's reaction chemistry would result in the same overalkylated impurities claimed by Applicants. Hoorn says nothing at all about the composition of any "reaction product

impurities" from the tamsulosin reaction scheme of Example 2A. Hoorn does not even describe what chemicals are being separated and what chemicals, other than tamsulosin, are being retained in the reaction material that is said in Example 2A to yield only 89.9% pure tamsulosin.

Since Applicants claim a different reaction chemistry using a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene over R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide as opposed to a molar excess of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide over 1-(2-bromoethoxy)- 2-ethoxybenzene, as said to have been the case in Hoorn in Example 2A, it cannot fairly be assumed that the amount or composition of whatever may have been the reaction impurities in Example 2A of Hoorn, if any, would be the same as what are called for in Applicants' claims. No person of ordinary skill would assume the same reaction product impurities, if any, in the same amount, when the relative amounts of the reactants are reversed from a molar excess of one, in the case of Hoorn, to a molar excess of the other, in Applicants' case. It is contrary to conventional wisdom and common sense to assume such.

No anticipation or obviousness rejection of a claim drawn to a purified reaction mixture with specifically delineated reaction impurities present in a measurable amount of less than 0.1% can validly be premised on an assumption that a prior art disclosure, in which the reactants are reacted in a materially different way with no disclosure of the "existence" of, much less the amount or composition of, any "impurities," would produce the same purified reaction mixture composition. Such an implausible result cannot be said to be anticipated, and it most certainly cannot be said to be "obvious."

No person of ordinary skill, who read Hoorn, would assume that the reaction of Hoorn, said to have been carried out in example 2A with a molar ratio of almost 2:1 of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide over 1-(2-bromoethoxy)- 2-ethoxybenzene to make, after certain purification steps, 89.9% pure tamsulosin, with no description of the amount or composition of any "impurities," would produce a purified reaction mixture containing a 99.5% pure tamsulosin and a measurable amount of specific overalkylated impurities, if the molar ratio of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide to1-(2-bromoethoxy)- 2-ethoxybenzene was reversed. In fact, nothing in Hoorn suggests that the molar ratio R-5-(2-

aminopropyl)-2-methoxybenzenesulphonamide to 1-(2-bromoethoxy)- 2-ethoxybenzene should be reversed, to begin with. And certainly nothing in Hoorn suggests that, should someone do something as major as reverse the molar excess of one reactant to the other, that, contrary to conventional wisdom, it would change nothing in terms of the composition of the reaction product. While nothing in Hoorn suggests doing so, it would nevertheless be apparent to a person of skill that he/she could not predict or expect the same reaction product mixture composition. While Hoorn does not suggest in Example 2A or otherwise the composition of any "impurities" by the Example 2A reaction scheme, the existence of a measurable amount of less than 1% of specifically claimed overalkylated impurities according to Claims 2, 15 and 16 in a 99.5% purified tamsulosin reaction mixture made by reacting a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene to R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide, instead of the reverse molar excess relationship as described in Example 2A of Hoorn, cannot reasonably be said to be anticipated or suggested by Hoorn.

The bottom line is that Hoorn does not disclose a reaction process for making tamsulosin that could reasonably be expected to make a purified tamsulosin reaction product mixture according to that claimed by Applicants, nor can it reasonably be said to suggest the same. Any way one looks at it, Applicants' claims patentably distinguish over Hoorn, and all rejections based thereon should be withdrawn.

II. New Claims 15 and 16.

Applicants have also introduced a new independent Claim 15 by this amendment. Claim 15 is directed to a crude reaction mixture, i.e., a reaction mixture which has not been purified by recrystallization or otherwise. This is in contrast to a purified mixture such as that recited in Claims 2 – 4. Claim 15 specifies that this crude reaction mixture comprises at least 75% tamsulosin hydrochloride and at least some measurable amount of overalkylated products, wherein said overalkylated products include N-(2-(2-ethoxyphenoxy)ethyl)-5-(2-(2-(2-ethoxyphenoxy)ethylamino) propyl)-2-methoxybenzenesulphonamide in an amount less than

5% by weight and 5-(2-(bis-(2-(2-ethoxyphenoxy)ethyl)amino)propyl)-2- methoxybenzene-sulphonamide in an amount less than 6 % by weight.

New Claim 16 is directed to a purified reaction product mixture generally in accordance with Claim 2 but without any reference to the method of making the same.

The subject matter of Claims 15 and 16 is also neither disclosed nor suggested by Hoorn or any other cited prior art.

In light of the foregoing, Applicants urge the Examiner to reconsider the application, to withdraw the rejections, and to issue a notice of allowance at the earliest possible convenience.

In the event that this response is not timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension, along with any other fees which may be due with respect to this response, may be charged to our Deposit Account No. 12-2355.

Respectfully submitted,

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